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EXAMINER	
CELSA, BENNETT M	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,034	STROOBANT, PAUL	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/26/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,17,19,20,23-48,50 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,17,19,20,23-48,50 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/02;4/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-53 are currently pending.

Claims 12-16, 18, 21-22, 49, 51 and 53 are withdrawn from consideration as being drawn to a nonelected invention.

Claims 1-11, 17, 19, 20, 23-48, 50 and 52 are under consideration.

Election/Restrictions

1. Applicant's election without traverse of the election of species in the reply filed on 10/26/04 is acknowledged. Applicant elected invention:

a. blood (Claims 10-11)

b. diseased/non-diseased (claim 17)

c. antibody (claims 19-21)

d. same array (claims 48, 50 and 52)

reads on claims 1-11, 17, 19, 20, 23-48, 50 and 52.

2. Claims 12-16, 18, 21-22, 49, 51 and 53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-11, 17, 19, 20, 23-48, 50 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. In claim 1 (and claims dependent thereon), the phrase "adhering a complex biological sample ... to a support to create an array" is indefinite as to how one adheres the entire sample (vs. its individual components) to create an array. In this respect, the claimed method is incomplete.

b. In the claims (e.g. claims 1, 3, 5, 6, and claims dependent thereon), the metes and bounds of the chemical composition of "a first product", "a second product", "a third product", "fourth product" , "a fifth product" or a "a sixth product" is unclear. There are no definitions regarding this terminology nor do the examples provide sufficient guidance regarding the metes and bounds of this terminology. Do the products encompass peptidic, nucleic, saccharide etc. structure or a complex thereof.

c. Claims 1-11, 17, 19, 20, 23-48, 50 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omit ting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step identifying a polypeptide which is recited in the preamble (e.g. of claim 1) and a treating step (e.g. of claim 27) involving treatment of the "the complex biological sample".

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-11, 17, 19, 20, 23-48, 50 and 52 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (lack of adequate written description).

It is first noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co*

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA

(encoding insulin)]. The *Lilly* court sets forth a two part test for written description:

A description of a genus of cDNA's may be achieved by means of a recitation of:

1. a representative number of cDNA's, defined by nucleotide sequence, falling within the scope of the genus Or

2. of a recitation of structural features common to the members of the genus.

See *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) at 1569.

The present claims are directed to a method of identifying a polypeptide comprising exposing "peptide-nucleic acid coupled library" to various complex biological sample arrays from different "types of individuals" to generate "first/second/third/fourth/fifth/sixth" products. The claims fail to provide any structure or properties regarding the variously claimed "genera" of :

a. "peptide-nucleic acid coupled library";

b. "types of individuals" ; and/or

c. "first/second/third/fourth/fifth/sixth" products

nor does the specification provide any concrete definition thereof or representative examples thereof. The specification examples are directed to specific separation protocols involving phage library capture (e.g. complexation) of immobilized proteins derived from healthy/sick individuals.

In the present instance, neither the specification nor the claims provide:

1. A recitation of structural features common to the members of the various " genera" *OR*

2. a representative number of species representative of the various genera.

As pointed out in the above, neither the specification nor claims recite structural and/or functional features or provide a representative number of species to demonstrate possession of these claimed generics.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-11, 17, 19, 20, 23-27, 33-36, 42-48, 50 and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Cai et al. PNAS USA Vol. 92, pages 6537-6541 (July 1995).

Present claim 1 is drawn to a method of identifying a polypeptide comprising:

a. adhering a "complex biological sample" from a first type of individual to a support to create an array;

b. adhering a complex biological sample from a second type of individual to a support to create an array;

c. exposing a "peptide-nucleic acid coupled library" at least one time to an array formed by step (a) to create a "first product"; and

d. exposing said first product at least one time to an array formed by step (b) to create a "second product".

Claim 2 reverses the order of claim 1 (e.g. by performing step b first and step a 2nd) to form "a third" and "fourth" product", respectively.

Claim 3 compares the "second" and "fourth" products respectively.

It is noted that the claims do not provide any structural or functional distinctions between the different recited products (e.g. first-sixth).

Cai et al. teach a method for identifying a "polypeptide" (e.g. antibodies or antigen markers) of normal vs tumor (e.g. melanoma) cells by adhering (e.g. culturing) "complex biological samples" (e.g. cells) from normal (e.g. healthy melanocytes) vs abnormal (e.g. tumor cells) which corresponds to steps a and b of present claim 1. Anti-melanoma antibodies were selected from each library by panning the phage against live cultures of the autologous tumour (e.g. from a "first type of individual" e.g. unhealthy) in which the complexed antibodies corresponding to a "first product". The panned phage population was extensively absorbed against normal melanocytes (e.g. "biological sample from a second type of individual e.g. healthy) to enrich for antibodies that react with melanoma cells but not with melanocytes (e.g. unabsorbed antibody library as "second product") which anticipated present claims 1, 8-11, 17, 19, 20, 23-24 . The

unabsorbed phage were amplified/cloned and tested (e.g. ELISA)against (e.g. exposing the library):

a. "a complex biological sample from a second type of individual (i.e. healthy such as normal endothelial and fibroblast cells) to identify antibodies that bind or those that don't (either of which corresponds to "a third product"); and

b. "a complex biological sample from a first type of individual (i.e. unhealthy such as melanocytes, several melanoma lines and eight other tumor lines) to identify antibodies that bind or those than don't (either of which corresponds to a "fourth product" but especially those that bind tumor antigens) thus anticipating present claims 2 (and claims dependent thereon). The reference teaches evaluating (e.g. ELISA) the test results of the above, including those of the "second" and "fourth" products (e.g. anticancer i.e. anti-melanoma antibodies) thus anticipating claim 3. The reference further teaches the identification (e.g. by ELISA) of different (e.g. three) classes of anti-melanoma antibodies from different patients; and the ***repeating of the above procedures*** utilizing the newly found anti-melanoma antibodies to screen the antibody repertoire of any person with cancer (or a person without cancer) which anticipates present claims 4-7 e.g. pooling and amplification of the product 2/4 anti-melanoma antibodies to screen first/second type (e.g. healthy/unhealthy) individuals forming "fifth" and "sixth" products, respectively. See Abstract; examples.

Claim Rejections - 35 USC § 103

9. Claims 1-11, 17, 19, 20, 23-27, 29-48, 50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cai et al. PNAS USA Vol. 92, pages 6537-6541 (July 1995) and Hutchens et al. US Pat. No. 6,225,047 (5/01: effectively filed 6/97).

Cai et al. teach a method for identifying a "polypeptide" (e.g. antibodies or antigen markers of normal vs tumor (e.g. melanoma) cells by adhering (e.g. culturing) "complex biological samples" (e.g. cells) from normal (e.g. healthy melanocytes) vs abnormal (e.g. tumor cells) (e.g. corresponds to steps a and b of present claim 1. Anti-melanoma antibodies were selected from each library by panning the phage against live cultures of the autologous tumour (e.g. from a "first type of individual" e.g. unhealthy)in which the complexed antibodies corresponding to a "first product" . The panned phage population was extensively absorbed against normal melanocytes (e.g. "biological sample from a second type of individual e.g. healthy) to enrich for antibodies that react with melanoma cells but not with melanocytes (e.g. unabsorbed antibody library as "second product") which anticipated present claims 1, 8-11, 17, 19, 20, 23-24 . The unabsorbed phage were amplified/cloned and tested (e.g. ELISA)against (e.g. exposing the library):

a. "a complex biological sample from a second type of individual i.e. healthy such as normal endothelial and fibroblast cells) to identify antibodies that bind or those that don't (either of which corresponds to "a third product"); and

b. "a complex biological sample from a first type of individual i.e. unhealthy such as melanocytes, several melanoma lines and eight other tumor lines) to identify

antibodies that bind or those than don't (either of which corresponds to a "fourth product" but especially those that bind tumor antigens. thus anticipating present claims 2 (and claims dependent thereon). The reference teaches evaluating the test results of the above ELISA's , including those of the "second" and "fourth" products (e.g. anticancer i.e. anti-melanoma antibodies) thus anticipating claim 3. The reference further teaches the identification (e.g. by ELISA) of different (e.g. three) classes of anti-melanoma antibodies from different patients; and the ***repeating of the above procedures*** utilizing the newly found anti-melanoma antibodies to screen the antibody repertoire of any person with cancer (or a person without cancer) which anticipates present claims 4-7 e.g. pooling and amplification of the product 2/4 anti-melanoma antibodies to screen first/second type (e.g. healthy/unhealthy) individuals forming "fifth" and "sixth" products, respectively. See abstract; examples.

The Cai et al. Reference teaching differs from the presently claimed invention by failing to disclose:

a. the use of a solid support with cross-linker attachment of analyte (e.g. claims 29-32);

b. use of mass spectrometry to analyze products (e.g. claims 37-41).

However, Hutchens teaches the favorable use of "rententate chromatography" which includes cross-linking analytes to solid supports and determining products by mass spectrometry when evaluating product components in assays involving different tissues (including healthy vs. diseased) and phage capture. See e.g. Figures 1-33

(especially figures 13-18; figures 21-29); col. 4 (especially lines 30-40; col. 5 (especially lines 40-45); col. 9, lines 10-50; col. 18-20; col. 36; examples and patent claims.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to modify the Cai reference method to cross-link analytes to solid supports and use mass spectometry to analyze products in order to optimize the Cai phage screening of tissue components in an analogous manner as in the Hutchen's reference.

10. Claims 1-11, 17, 19, 20, 23-48, 50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cai and Hutchens et al. as applied to claims 1-11, 17, 19, 20, 23-27, 29-48, 50 and 52 above, and further in view of Cull et al., Methods in Enzymology Vol. 182:147-238.

The Cai et. al. and Hutchens Reference teachings described above in the obviousness rejection is hereby incorporated by reference in its entirety. The Cai et al teaching separately, or combined with Hutchens, differs from the presently claimed invention by failing to teach denaturation of the complex biological sample prior to adhering to a support to create an array (e.g. claim 28).

However, Cull et al. teaches that preliminary processing of biological samples, including the use of preliminary separation techniques and/or denaturation, may be desirable in order to effect better analyte (e.g. peptide) purifications and/or use in subsequent screening.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to incorporate a denaturation step into the Cai method (or when combined with Hutchen) prior to attachment and/or adherence of the biological sample to the support in order to optimize analyte purification and/or its subsequent screening.

Relevant Prior Art:

1. Gron et al., FEBS Lett. Vol. 391 (1996) pages 71-75.

2. Holt et al. Current Opinion in Biotechnology 2000 Vol. 11 pages 445-449.

3. De Kruif et al., PNAS USA Vol. 92 (April 1995) pages 3938-3942.

4. Paweletz et al., Drug Develop. Vol. 49 (2000) pages 34-42 (of record in IDS).

5. de Wildt et al., Nature Biotechnology (Sept. 2000) pages 989-994 (of record in IDS).

6. WO 99/39210 (of record in IDS).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

January 21, 2005
BC